



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,363	11/13/2000	David Eisenberg	07419-032001 / LA99-566-6	9082

7590 12/30/2003
Gregory P Einhorn
Fish & Richardson PC
Suite 500
4350 La Jolla Village Drive
San Diego, CA 92122

EXAMINER

STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/712,363

Applicant(s)

EISENBERG ET AL.

Examiner

Teresa E Strzelecka

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20, 22-30 and 34-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13, 18-20, 34 and 35 is/are rejected.
- 7) ☒ Claim(s) 12, 14-17, 22-30 and 36 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. This office action is in response to an amendment filed on August 27, 2003. Claims 1-20, 22-30 and 34-36 were pending. Applicants amended claims 2, 6, 9, 11-13, 19, 20, 24, 28, 29 and 34-36.
2. Applicants' amendments overcame the rejection of claims 1-20, 22-30 and 34-36 under 35 U.S.C 112, second paragraph.
3. This office action is made non-final because of new grounds for rejection.

Claim interpretation

4. The term "biological or chemical property of interest" is interpreted as any property of a protein.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 34, 35, 1-5, 7-9, 11 and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Tatusov et al. (Curr. Biol., vol. 6, pp. 279-291, 1996) as evidenced by Koonin et al. (PNAS, vol. 92, pp. 11921-11925, 1995).

Regarding claim 34, Tatusov et al. teach functional identification of H. influenzae proteins (= a set of second proteins) by comparison of two genomes: H. influenzae and E. coli, the method comprising:

(a) providing a first nucleic acid sequence that encodes a first protein or a first polypeptide sequence of the first protein wherein the first protein has a biological or chemical property of

Art Unit: 1637

interest (Tatusov et al. teach providing 3010 E. coli protein sequences (= a set of first polypeptide sequences), which possess biological and chemical properties of interest, for example, being involved in amino-acid metabolism (Abstract; page 281, second paragraph; Table 1);

(b) providing at least one algorithm capable of analyzing a functional relationship between the first protein and second protein, wherein the algorithm is selected from the group consisting of a "domain fusion" method, a "phylogenetic profile" method, and a "physiologic linkage" method (Tatusov et al. teach both the phylogenetic profile method and the physiologic linkage method; see details below for claims 9 and 18); and

(c) comparing the first nucleic acid sequence or the first polypeptide sequence to a plurality of sequences using at least one of the algorithms as set forth in step (b) to identify the second nucleic acid sequence or second polypeptide sequence of the second protein which has a functional relationship to the first protein, thereby identifying a second nucleic acid sequence or a second polypeptide sequence of a second protein that possesses the property of interest (Tatusov et al. teach comparing the E. coli protein sequences to the H. influenzae proteins (= a set of second nucleic acid proteins) and identifying functions of H. influenzae proteins which have the same properties of interest as the E. coli proteins (Table 5)).

Regarding claim 35, Tatusov et al. teach, for example, glycolysis proteins which have glucose binding sites (property of interest being binding and catalysis of glucose), and outer membrane proteins (property of interest being cellular localization).

Regarding claim 1, Tatusov et al. teach multidrug resistance proteins (see page 7 of a table printed from the NCBI web site (referred to as Table-NCBI), which is referenced in the last paragraph on page 290), a penicillin-binding protein, mrca (page 33 of the Table-NCBI).

Regarding claim 2, Tatusov et al. teach glycolysis proteins, which are essential for growth and viability of the organism (Table 5).

Regarding claim 3, Tatusov et al. teach a penicillin-binding protein, mrca (page 33 of the Table-NCBI), which is a target for an antimicrobial drug.

Regarding claims 4 and 5, Tatusov et al. teach first proteins derived from E. coli, which is a pathogen and a microorganism.

Regarding claims 7 and 8, Tatusov et al. teach a plurality of second sequences comprising an entire genome of a pathogen, H. Influenzae (Abstract; page 279, first paragraph; page 280, second paragraph).

Regarding claim 9, Tatusov et al. teach a “phylogenetic profile” method, comprising:

(a) obtaining data, comprising a plurality of sequences, wherein the plurality of sequences comprises a list of polypeptide sequences of proteins from at least two genomes or a list of nucleic acid sequences that encode proteins from at least two genomes (Tatusov et al. teach obtaining a plurality of protein sequence from two genomes, E. coli and H. influenzae (Abstract; page 280, first paragraph; page 290, third and fourth paragraphs).);

(b) determining a protein phylogenetic profile for the first protein and for each protein of the plurality of sequences, wherein the protein phylogenetic profile indicates the presence or absence of a protein belonging to a particular protein family in each of the at least two genomes wherein the presence or absence of a protein in a particular protein family is determined by homology (Tatusov et al. teach homology alignment of proteins and detection of proteins with significant sequence similarity (page 290, fifth paragraph).);

(c) grouping the proteins of the plurality of sequences based on similar profiles, wherein proteins with similar profiles are indicated to have a functional relationship (Tatusov et al. teach

that the proteins identified by homology were then clustered based on linkage analysis and pre-determined cut-off values ((page 290, sixth paragraph), identifying families of proteins with similar function (page 280, fifth paragraph; Table 1).; and

(d) comparing the first nucleic acid sequence or the first polypeptide sequence to the plurality of sequences by comparing the protein phylogenetic profile for the first protein to the protein phvlogenetic profiles of the plurality of sequences to identify the second protein, whereby the second protein is selected from the members of the group with similar profiles as the first protein (Tatusov et al. teach comparing the E. coli protein sequences to the H. influenzae proteins (= a set of second nucleic acid proteins) and identifying functions of H. influenzae proteins which have the same properties of interest as the E. coli proteins (Table 5)).

Regarding claim 11, Tatusov et al. teach using a cutoff value of 90 in BLASTP alignments as indicating significant homology, but does not specifically teach using a probability value threshold. As evidenced by Koonin et al, the cutoff value of 90 in BLASTP indicates the probability of match by chance of 0.001 (page 11922, third full paragraph), therefore Tatusov et al. teach the limitation of claim 11.

Regarding claim 18, Tatusov et al. teach identifying proteins which participate in a common functional pathway, for example, TCA cycle, pentose phosphate pathway, arginine biosynthesis, etc. (Table 5).

Regarding claim 19, Tatusov et al. teach identifying proteins which participate in the synthesis of a common structural complex, for example, arginine biosynthesis, pyrimidine biosynthesis, etc. (Table 5).

Regarding claim 20, Tatusov et al. teach identifying proteins which participate in a common metabolic pathway, for example, TCA cycle, nitrogen assimilation cycle, etc. (Fig. 5).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tatusov et al. and Philipp et al. (PNAS, vol. 93, pp. 3132-3137, 1996).

A) The teachings of Tatusov et al. are described above. Tatusov et al. teach comparison of two pathogen sequences, but do not teach one of the being *Mycoplasma tuberculosis*.

B) Philipp et al. teach that genome research and systematic sequence analysis are necessary for *M. tuberculosis* (page 3132, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the *M. tuberculosis* genome in the method of Tatusov et al. The motivation to do so, provided by Philipp et al., would have been that "In spite of the availability of effective short-course chemotherapy, and the bacillus Calmette-Guérin (BCG) vaccine, *Mycobacterium tuberculosis* still accounts for more deaths worldwide than any other single infectious agent" (page 3132, first paragraph).

9. Claims 10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tatusov et al. and Dandekar et al. (TIBS, vol. 23, pp. 324-328, September 1998).

A) Teachings of Tatusov et al. are described above. Tatusov et al. teach determining phylogenetic profiles of proteins, but do not teach phylogenetic trees, vectors or matrices or calculation of an evolutionary distance.

B) Dandekar et al. teach construction of phylogenetic trees by comparison of genomes of *Escherichia coli*, *haemophilus influenza*, *Helicobacter pylori*, *M. genitalium*, *M. pneumoniae*, *Bacillus subtilis*, *Methanococcus jannaschii*, *Methanobacterium thermoautotropicum* and *Archeoglobus fulgidus*. The phylogenetic tree was based on calculating the evolutionary distances. (Fig. 1; page 324, second paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used evolutionary distance calculations and phylogenetic trees of Dandekar et al. in the method of Tatusov et al. The motivation to do so, provided by Dandekar et al., would have been that analysis of phylogenetic trees based on evolutionary distances provided information about conservation of gene order, which was used to predict functions of and interactions between proteins (Abstract; page 324, last paragraph; page 325, second paragraph; page 327, paragraphs 4-7).

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claim 34 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,466,874.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 34 of the instant application is generic to all that is recited in claims 1 and 2 of U.S. Patent No. 6,466,874. That is, claims 1 and 2 of the U.S. Patent No. 6,466,874 fall entirely within the scope of claim 34, or, in other words, claim 34 is anticipated by claims 1 and 2 of U.S. Patent No. 6,466,874. Specifically, the method of claim 34 is drawn to identification of a functional relationship between two proteins using an algorithm selected from the group consisting of a "domain fusion" method, a "phylogenetic profile" method and a "physiologic linkage" method, whereas claims 1 and 2 of the U.S. Patent No. 6,466,874 are drawn to a "domain-fusion" method.

12. Claim 34 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 19 of U.S. Patent No. 6,564,151.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 34 of the instant application is generic to all that is recited in claims 1 and 2 of U.S. Patent No. 6,564,151. That is, claims 1 and 19 of the U.S. Patent No. 6,564,151 fall entirely within the scope of claim 34, or, in other words, claim 34 is anticipated by claims 1 and 19 of U.S. Patent No. 6,564,151. Specifically, the method of claim 34 is drawn to identification of a functional relationship between two proteins using an algorithm selected from the group consisting of a “domain fusion” method, a “phylogenetic profile” method and a “physiologic linkage” method, whereas claims 1 and 19 of the U.S. Patent No. 6,564,151 are drawn to a “phylogenetic profile” method.

13. Claim 34 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of copending Application No. 09/493,401.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 34 of the instant application is generic to all that is recited in claim 3 of the copending Application No. 09/493,401. That is, claim 3 of the copending Application No. 09/493,401 fall entirely within the scope of claim 34, or, in other words, claim 34 is anticipated by claim 3 of copending Application No. 09/493,401. Specifically, the method of claim 34 is drawn to identification of a functional relationship between two proteins using an algorithm selected from the

Art Unit: 1637

group consisting of a "domain fusion" method, a "phylogenetic profile" method and a "physiologic linkage" method, whereas claim 3 of the copending Application No. 09/493,401 is drawn to a "domain-fusion" method and "phylogenetic profile" method combined.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. No references were found teaching or suggesting claims 12, 14-17, 22-30 and 36. Claims 12, 14-17, 22-30 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

The examiner will move to the new office in Alexandria on January 8, 2004. The new phone number in that office is (571) 272-0789. Gary Benzion will move to the new office on January 22, 2004. His new phone number is (571) 272-0782.


JEFFREY FREDMAN
PRIMARY EXAMINER

TS
December 21, 2003

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

